Human T lymphotropic virus types 1 and 2: a point of view

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Reported at the beginning of the 1980s, Human T lymphotropic viruses type 1 and 2 (HTLV1, HTLV 2) were the first retroviruses to have been detected in human beings. HTLV 1 was isolated from adult T-cell leukemia (ATL) and first described by Takatsuki et al. in Japan in 1976, as a malignancy that only affects T cells and only in adults[1,2].

Albeit infrequent, HTLV-1 infection may lead to severe morbidity when it causes malignancy or degenerative conditions. The virus can also cause mild immune deficiency even in the absence of any malignancy. Fatal neurologic diseases, such as HTLV-associated myelopathy/tropical spastic paraparesis (HAM/TSP), uveitis, iritis, peripheral neuropathies, and arthritis can also be caused by HTLV-1. All these diseases can be autoimmune, but their exact mechanisms are not yet known[3]. Human T lymphotropic virus type 2 (HTLV-2) was discovered in a patient with a T-cell variant of hairy cell leukemia. The virus has been associated with increased mortality and morbidity, risk for pneumonia and bronchitis, urinary tract infections, and rare neurologic manifestations. HTLV infection is life-long and disease symptoms can manifest some 20-40 years post-infection[4-6]. Recently, an increased prevalence of psychiatric symptoms was described among HTLV-seropositive patients[7,8].

Prevalence greatly varies in different regions of the world. HTLV-1 is endemic in southwestern Japan, in the Caribbean Islands, and in Central Africa. Carriers have been identified in South America, Papua New Guinea, the Solomon Islands, South China, and other isolated populations such as the Australia Aborigines. HTLV-2 can also be found in some Native American populations. HTLV-1 is transmitted by blood, through sexual contact, injectable drug use and from mother to offspring through breastfeeding[1-6]. HTLV-2 is most often found in injectable drug users and in their sexual partners.

As a consequence of the transmission routes, all blood donated at the Red Cross Blood Centers in Japan has been subjected to HTLV-1 antibody screening since November 1986 and carrier mothers have been instructed to refrain from breastfeeding to prevent HTLV-1 transmission[9-11]. In the United States, screening began at the end of 1988 and in the entire world since 1990[12-15]. At the beginning, blood donor screening was performed with enzyme immunoassays (EIAs) for antibodies against HTLV-1 and later against HTLV-1/2, which led to the unnecessary deferral of a great number of individuals. Confirmatory testing could be performed by Western blot but this was expensive and took a long time. Nowadays screening is performed by chemiluminescent immunoassay with a lower risk of false positives[16]. Up to now there is no available licensed confirmatory test. The efficacy of this test reduces the number of indeterminate results and could be better than the lookback procedure for HTLV-1/2[17]. Confirmatory testing by polymerase chain reaction (PCR), albeit expensive, is used in the great majority of blood banks around the world. The same serological difficulties are observed in Brazil as confirmatory testing is only performed by research groups in some blood banks. HTLV-1/2 infection is endemic in Brazil[18-22] and testing blood donors has been mandatory since 1993.

Recently, Carneiro-Proentti et al.[22] analyzed all blood donations of three regional Brazilian Blood Banks located in São Paulo, Minas Gerais and Pernambuco during 2007-2009. Serological results were confirmed by Western blot. Results concerning donor age, gender, education status, and race confirmed the previously published results from other Brazilian blood banks[23,25]. Prevalence increased with age, was higher among women and Blacks and was inversely correlated to the level of education. Prevalence variations in different blood banks were expected and probably reflect population origins (higher in Pernambuco than in Sao Paulo and Minas Gerais).

The overall incidence rate was 3.59 per 100,000 person-years and the residual risk was 5.0/100,000 per repeat donor blood unit transfused, that is, lower than previously reported in southern Brazil[25]. Seroprevalence rates were in the order of 1 to 2 per thousand first time donors which is higher than in the United States and Europe but lower than in the Brazilian general population[24].

Besides HTLV screening difficulties, the public health system is also not prepared to confirm and counsel serum-positive donors thus creating a difficult situation as the virus can be

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transmitted through breastfeeding and the disease can appear almost 30 years after a serological positive result. Preventive measures, the follow up of donors and confirmatory testing procedures must be improved.

In this issue of the *Revista Brasileira de Hematologia e Hemoterapia*, Lima et al. bring new data from the Caruaru Blood Center in Pernambuco[26].

References

1. Takatsuki K. Discovery of adult T-cell leukemia. Retrovirology. 2005;2:16 Comment in: Retrovirology. 2005;2:15.
2. Gallo RC. History of the discoveries of the first human retroviruses: HTLV-1 and HTLV-2. Oncogene. 2005;24(39):5926–30.
3. Gallo RC. The discovery of the first human retrovirus: HTLV-1 and HTLV-2. Retrovirology. 2005;2:17. Comment in: Retrovirology. 2005;2:15
4. Gallo RC. Research and discovery of the first human cancer virus, HTLV-1. Best Pract Res Clin Haematol. 2011;24(4):559-65.
5. Yoshida M. Discovery of HTLV-1, the first human retrovirus, its unique regulatory mechanisms, and insights into pathogenesis. Oncogene. 2005;24(39):5931-7.
6. Guiltinan AM, Kaidarova Z, Behan D, Marosi C, Hutching S, Kaiser M, Moore E, Devita D, Murphy EL; HTLV Outcomes Study (HOST). Major depression and generalized anxiety disorder among human T-lymphotropic virus types I- and II-infected former blood donors. Transfusion. 2013;53(1):60-8.
7. Carvalho AG, Galvão-Phileto AV, Lima NS, Jesus RS, Galvão-Castro B, Lima MG. Frequency of mental disturbances in HTLV-1 patients in the state of Bahia, Brazil. Braz J Infect Dis. 2009;13(1):5-8.
8. Hino S. Establishment of the milk-borne transmission as a key factor or the peculiar endemicity of human T-lymphotropic virus type 1 (HTLV-1): the ATL Prevention Program Nagasaki. Proc Jpn Acad Ser B Phys Biol Sci. 2011;87(4):152-66.
9. Pimenta FC, Kashima Haddad S, de Medeiros Filho JG, Costa MJ, Diniz MF, Fernandes MP, et al. Prevalence ratio of HTLV-1 in nursing mothers from the state of Paraiba, Northeastern Brazil. J Hum Lact. 2008;24(3):289-92.
10. Ribeiro MA, Proietti FA, Martins ML, Januário JN, Ladeira RV, Oliveira M de F, et al. Geographic distribution of human T-lymphotropic virus types 1 and 2 among mothers of newborns tested during neonatal screening, Minas Gerais, Brazil. Rev Panam Salud Publica. 2010;27(5):330-7.
11. Vrielink H, Zaaijer HL, Reesink HW. The clinical relevance of HTLV type I and II in transfusion medicine. Transfus Med Rev. 1997;11(3):173-9.
12. Davison KL, Dow B, Barbara JA, Hewitt PE, Eglin R. The introduction of anti-HTLV testing of blood donations and the risk of transfusion-transmitted HTLV, UK: 2002-2006. Transfus Med. 2009;19(1):24-34.
13. Rafatpanah H, Hedayati-Moghaddam MR, Fathimoghadam F, Bidkhori HR, Shamsian SK, Ahmadi S, et al. High prevalence of HTLV-I infection in Mashhad, Northeast Iran: a population-based seroepidemiology survey. J Clin Virol. 2011;52(3):172-6.
14. Laperche S, Worms B, Pillonel J; European Network of Transfusion Medicine Societies; Steering Committee. Blood safety strategies for human T-cell lymphotropic virus in Europe. Vox Sang. 2009;96(2):104-10.
15. Stramer SL, Notari EP 4th, Zou S, Krysztof DE, Brodsky JP, Tegtmeier GE, et al. Human T-lymphotropic virus antibody screening of blood donors: rates of false-positive results and evaluation of a potential donor reentry algorithm. Transfusion. 2011;51(4):692-701. Comment in: Transfusion. 2011;51(4):668-9.
16. Stramer SL, Foster GA, Dodd RY. Effectiveness of human T-lymphotropic virus (HTLV) recipient tracing (lookback) and the current HTLV-I and -II confirmatory algorithm, 1999 to 2004.Transfusion. 2006;46(5):703-7.
17. Castro-Costa CM, Vale OC, Goubau P, Desmyter J, Carton H. HTLV-I and tropical spastic paraparesis in Fortaleza (Northeastern Brazil). J Trop Geogr Neurol. 1991;1:45-8.
18. Galvão-Castro B, Proietti F, Rodrigues L, Franco F, Santana A, Loures L. HTLV-I/II differential geographic distribution in Brazil. In: 10th International Conference on AIDS, 1994. Yokohama, Japan, 7-12 August.
19. Yamashita M, Veronesi R, Menna-Barreto M, Harrington WJ Jr, Sampio C, Brites C, et al. Molecular epidemiology of human T-cell leukemia virus type I (HTLV-1) Brazil: the predominant HTLV-1s in South America differ from HTLV-ls of Japan and Africa, as well as those of Japanese immigrants and their relatives in Brazil. Virology. 1999;261(1):59-69.
20. Dourado I, Alcantara Jr LC, Barreto ML, Teixeira MG, Galvão-Castro B. HTLV-I in the general population of Salvador, Brazil: a city with African ethnic and sociodemographic characteristics. J Acquir Immnue Defic Syndr. 2003;34(5):527-31.
21. Laurentino RV, Lopes IG, Azevedo VN, Machado LF, Moreira MR, Lobato L, et al. Molecular characterization of human T-cell lymphotropic virus coinfecting human immunodeficiency virus 1 infected patients in the Amazon region of Brazil. Mem Inst Oswaldo Cruz. 2005;100(4):371-6.
22. Carneiro-Proietti AB, Sabino EC, Leão S, Salles NA, Loureiro P, Sarr M, Wright D, Busch M, Proietti FA, Murphy EL; NHLBI Retrovirus Epidemiology Donor Study-II (Reds-II), International Component. Human T lymphotropic virus type 1 and type 2 seroprevalence, incidence, and residual transfusion risk among blood donors in Brazil during 2007–2009. AIDS Res Hum Retroviruses. 2012;28(10):1265-72.
23. Catalan-Soares B, Carneiro-Proietti AB, Proietti FA; Interdisciplinary HTLV Research Group. Heterogeneous geographic distribution of human T-cell lymphotropic viruses I and II (HTLV-I/II): serological screening prevalence rates in blood donors from large urban areas in Brazil. Cad Saude Publica. 2005; 21(3):926-31.
24. Dias-Bastos MR, Oliveira CD, Carneiro-Proietti AB. Decline in prevalence and asymmetric distribution of human T cell lymphotropic virus 1 and 2 in blood donors, State of Minas Gerais, Brazil, 1993 to 2007. Rev Soc Bras Med Trop. 2010;43(6):615-9.
25. Maresch C, Schluter PJ, Wilson AD, Sleigh A. Residual, infectious disease risk in screened blood transfusion from a high-prevalence population: Santa Catarina, Brazil. Transfusion. 2008;48(2):273-81.
26. Lima WM, Esteves FA, Torres MC, Pires ES. Prevalence of human T-cell lymphotropic virus types 1 and 2 in blood donors of the Caruaru Blood Center (Hemope). Rev Bras Hematol Hemoter. 2013;35(4):268-71.